

## **REMARKS**

### **Rejections Under 35 U.S.C. § 112**

The rejections are overcome by the amendments. Support for the amendment to claim 5 can be found, for example, on page 16, of the specification. Support for the amendment to claim 15 can be found, for example, on page 21, of the specification.

Claim 23 is rewritten in independent form.

### **Rejections Under 35 U.S.C. § 103**

Claims 1-5, 7, 10, 11, 13-16, 18-20, 22 and 23 have been rejected as allegedly unpatentable over Schollkopf et al. (WO 96/20209) and Backensfeld et al. (U.S. Patent No. 798,338) in view of Schollkopf et al. (WO 96/20209) in view of Hedges (Chem. Rev., 1998).

Applicants maintain that the combination of the references does not render the claims obvious. But, in order to further prosecution, applicants provide further evidence of unexpected results. This evidence will be submitted in a supplemental declaration in the near future.

The first table shown below in the declaration demonstrates that the compound ZK 187226, without it being combined with excipients for tableting, is stable. That is, no substantial degradation is present. One of ordinary skill in the art in view of such data would have lacked the motivation to combine ZK 187226 with compounds taught to stabilize gestagens since this gestagen on its own is stable. One of ordinary skill in the art prior to even trying to stabilize ZK 187226, would have checked whether ZK 187226 needs to be stabilized. Since ZK 187226 is stable, the rejection presents no motivation that would lead one of ordinary skill in the art to combine ZK 187226 with a cyclodextrin as claimed.

*The following table provides stability data for ZK 187226 without it being combined with excipients for tableting.*

Months	25°C/60% rel. hum. content %	30°C/35% rel. hum. content %	25°C/60% rel. hum. content %
0	100		
1			99.9
3	99.0	99.6	99.1
6	98.7	99.3	98.1
9	98.6	96.5	terminated
12	98.0	99.0	

The second table shown below demonstrates that once ZK 187226 is combined with common excipients (and without cyclodextrins), it degrades due to acyloin rearrangement. See also specification on pages 1 and 2. The data for this second table are calculations of percentages of the decomposition products from the data curves already submitted in graphical format in the previous declaration. Two groups of decomposition products are calculated in addition to the amount of ZK 187226. The first group constitutes compounds that have a retention time between 3 and 13 minutes, the structure of which compounds is unknown, and the second group is the sum of ZK 187225, ZK 187929, and ZK 187928, which are decomposition products known to be due to acyloin rearrangement of ZK 187226.

*The following table provides stability data for ZK 187226 in tablets with common excipient, but without cyclodextrins after 6 weeks of storage. The tablets contain 0.1 mg of ZK 187226.*

	sum of peaks between retention time 3 to 13 min (% area)	ZK 187226 (% area)	Sum of ZK 187225, ZK 187929, ZK 187928 (% area)
25°C	2.2	91.3	6.5
40°C	21.9	36.9	41.2
60°C	94.2	1.2	4.6
25°C/60% rel. hum.	4.5	83.7	11.8
40°C/75% rel. hum.	37.7	44.1	18.2
60°C/75% rel. hum.	97.3	0.8	2.0

As noted above, the structure of the compounds with a retention time between 3 and 13 minutes is unknown. However, ZK 187226, when, by itself, does not decompose to these products as demonstrated in the first table. In any event, one of ordinary skill in the art seeing from the second table that at least a large part of the degradation is due to acyloin rearrangement of the gestagen ZK 187226, would not have been motivated to combine the same with a cyclodextrin taught to affect degradation due to oxidation.

The third table shown below demonstrates significant stabilization of ZK 187226 from acyloin rearrangement in a tablet when combined with cyclodextrins. This significant reduction in acyloin rearrangement of ZK 187226 is unexpected from the prior art, and thus, supports patentability of the claimed invention.

*The following table provides stability data for ZK 187226 in tablets with cyclodextrins after 6 weeks of storage. The tablets contain 0.1 mg of ZK 187226.*

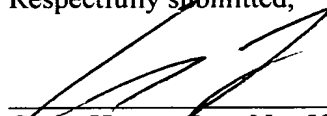
	sum of all peaks between retention time 3 to 13 min (% area)	ZK 187226 (% area)	sum of ZK 187225, ZK 187929, ZK 187928 (% area)
25°C	1.0	98.9	0.1
40°C	1.2	98.5	0.3
60°C	3.8	96.0	0.2
25°C/60% rel. hum.	1.0	98.8	0.2
40°C/75% rel. hum.	2.0	97.3	0.7
60°C/75% rel. hum.	5.0	94.6	0.4

Additionally, claim 23, now independent, is not taught or suggested by the prior art.

Reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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